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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/951,188	10/15/1997	DAVID H. PRICE	IOWA-012/FUS	1309

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EXAMINER

STEADMAN, DAVID J

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 03/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.

08/951,188

Applicant(s)

PRICE, DAVID H.

Examiner

David J. Steadman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 110-113, 116-164, 167-172, 174-208 and 211-216 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 110, 113, 116-127, 133-143, 147-155, 157-164, 167-172, 174-208 and 211-216 is/are rejected.
- 7) ☒ Claim(s) 111, 112, 128-132, 144-146 and 156 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Application Status

[1] A decision to withdraw the finality of the Office action of Paper No. 16 is acknowledged and has been entered as Paper No. 19. In view of the Decision of the Petition of Paper No. 17 to withdraw finality of the Office action of Paper No. 16, the finality of that action is withdrawn.

[2] Claims 110-113, 116-164, 167-172, 174-208, and 211-216 are pending in the application.

[3] Applicants' cancellation of claims 114, 115, 165, 166, 173, 209, and 210 and amendment to claims 110, 113, 116-125, 137, 152, 157, 164, 168, 174-177, 181-183, 185, 190, 194, and 203-207 in Paper No. 20, filed 08/27/01, is acknowledged.

[4] Applicants' arguments presented in Paper No. 20 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Interview

[6] It is noted that applicants state that a telephonic interview was conducted on 08/22/01 between Ms. Shelley Fussey and examiner Tung. It appears that, based on applicants' statements, Examiner Tung had indicated withdrawal of rejections and/or possible allowance of the claims based on proposed amendments discussed during the interview. Applicants further state that Examiner Tung would contact applicants to revise any non-allowable claims by examiner's amendment to place the claims in a condition for allowance. It is noted that, aside from applicants' statements, there is no record this interview in the instant application. It is further noted that the instant application has been transferred to Examiner Steadman. While applicants' response overcomes some of the previous rejections, it is the examiner's view that the remaining issues warrant a formal Office action.

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Claim Rejection(s) - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[7] Claims 137-148, 157-164, and 167-216 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[8] Claim 137 (claims 138-148 and 198-207 dependent therefrom) are indefinite in the recitation of "P-TEFb kinase subunit". It is unclear from the claims and the specification as to the scope of kinase proteins referred to in the claims. It is suggested that applicants clarify the meaning of the claim by, for example, providing distinguishing characteristics of a P-TEFb kinase, e.g., a sequence identifier.

[9] Claim 137 (claims 138-148 and 198-207 dependent therefrom) recites the limitation "the nucleotide sequence of: the coding sequence". There is insufficient antecedent basis for this limitation in the claim. It is suggested that the term be replaced with, for example, "a nucleotide sequence of: a coding sequence".

[10] Claims 137 (claims 138-148 and 198-207 dependent therefrom), 181 (claims 184-189, 194-197, and 208-216 dependent therefrom), 190 (claims 191-193 dependent therefrom) are indefinite in the recitation of "probe". The specification defines the term "probe" at page 67, lines 14-16. However, it is unclear from this definition as to the nucleotide length of the probe. It is suggested that applicants clearly indicate the length of the "probe". For purposes of examination, the term has been interpreted as a probe of less than 21 nucleotides. This interpretation has been made in light of dependent claim 138.

[11] Claims 157-164, 167-197, and 208 (claims 209-216 dependent therefrom) are unclear in the recitation of the term "expression system". An expression system typically refers to an expression vector *and* a compatible host cell. However, in this case, it appears from, e.g., claim 180, that the term "expression system" does not encompass a host cell. It is suggested that applicants clarify the meaning of the claims, by for example, replacing the term "expression system" with "expression vector".

Claim Rejection(s) - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[12] Claims 110, 113, 116-127, 133-143, 147, 148, 157-164, 167, 168, 178-205, 208, and 211-216 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

- Claims 110, 113 (claims 133-136 and 198-202 dependent therefrom), 116-127, 203, and 204 are drawn to a genus of nucleic acids or host cells comprising a nucleic acid sequence encoding fragments of SEQ ID NO:4, 45, 47, or 50.
- Claims 137 (claims 198-202 dependent therefrom) 138-143, 147, 148, and 205 are drawn to genus of nucleic acids or host cells comprising a nucleotide sequence of a cDNA molecule that hybridizes to a probe that is the complement of SEQ ID NO:3, 43, or 48 under the recited hybridization conditions encoding a P-TEFb large subunit protein, wherein the nucleic acid has an undefined sequence (claims 137, 147, and 148) or comprises fragments of SEQ ID NO:3, 43, or 48 (claims 138-143).
- Claims 157 (claims 178-180 and 208-216 dependent therefrom), 158-164, 167, and 168 are drawn to a genus of expression vectors or host cells comprising a second nucleic acid comprising a nucleic acid sequence comprising the nucleic acids of claims 137 and optionally fragments or homologues of SEQ ID NO:4, 45, 47, or 50 as set forth in claims 164, 167, and 168, and 177.
- Claims 181 (claims 195-197 and 208-216 dependent therefrom) and 182-194 are drawn to a genus of expression vectors comprising a first nucleic acid comprising all nucleic acids comprising a coding sequence of a cDNA that hybridize to an undefined number of nucleotides or the recited fragments of the complement of SEQ ID NO:1 or 5 *and* a second nucleic acid comprising a nucleic acid

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sequence comprising the nucleic acids of claims 137 or 149 and optionally variants and fragments of SEQ ID NO:4, 45, 47, or 50 and homologues of SEQ ID NO:3, 43, or 48.

Claims 110, 113, 116-127, 203, and 204 are rejected because the function of the genus of claimed nucleic acids has not been adequately described in the specification. The genus of nucleic acids encoding proteins comprising fragments of SEQ ID NO:4, 45, 47, or 50 encompasses many nucleic acids encoding different proteins having distinct functions. Therefore, substantial functional variation exists within the genus. The disclosed nucleic acids provided in the specification fail to provide a representative number of species sufficient to describe the entire genus of claimed nucleic acids. Thus, this disclosure is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus.

Claims 137, 143, 147, 148, 157 part (b), 164, 167, 168, 181 parts (a) and (b), 182, 183, 185, 190, and 205 are rejected because the structures of the species within the genus of claimed nucleic acids has not been adequately described in the specification. The Federal Circuit (*UC California v. Eli Lilly*, (43 USPQ2d 1398)) has said that a sufficient written description of a genus of nucleic acids may be achieved by recitation of a representative number of nucleic acids defined by nucleotide sequence or a recitation of structural features common to members of the genus, *which features constitute a substantial portion of the genus*. The recited structural features of the genus of claimed nucleic acids *does not* constitute a substantial portion of the genus as the remainder of the structure of a polypeptide having the recited activity is *completely undefined*. The specification does not define the remaining structural features necessary for a polypeptide encoded by the species of the claimed genus of nucleic acids to be selected.

Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

[13] Claims 110, 113, 116-127, 133-143, 147-155, 157-164, 167-208, and 211-216 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the entire scope of the claims.

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- Regarding claims 110 (claims 198-202 dependent therefrom), 113 (claims 133-136 and 198-202 dependent therefrom), 116-127, 203, and 204, the specification, while being enabling for a nucleic acid encoding SEQ ID NO:4, 45, 47, and 50, does not reasonably provide enablement for all nucleic acids comprising a nucleic acid sequence encoding the recited fragments of SEQ ID NO:4, 45, 47, and 50.
- Regarding claims 137 (claims 198-202 dependent therefrom), 138-143, 147, 148, and 205, the specification, while being enabling for the nucleic acids of SEQ ID NO:3, 43, and 48, does not reasonably provide enablement for all nucleic acids comprising a coding sequence of a cDNA that hybridize to an undefined number of nucleotides or the recited fragments of the complement of SEQ ID NO:3, 43, or 48 and encoding a P-TEFb large subunit.
- Regarding claims 149 (claims 198-202 dependent therefrom), 150, 151, and 206, the specification, while being enabling for a nucleic acid encoding SEQ ID NO:4, 45, 47, and 50, does not reasonably provide enablement for all nucleic acids comprising a nucleic acid sequence encoding any P-TEFb large subunit that is at least 90%, 91-95%, or 96-99% identity to SEQ ID NO:4, 45, 47, and 50, wherein the encoded protein binds to any P-TEFb kinase to form an enzyme complex that promotes transcription elongation.
- Regarding claims 152 (claims 198-202 dependent therefrom) 153-156, and 207, the specification, while being enabling for a nucleic acid comprising a first nucleic acid encoding SEQ ID NO:2 or 6 *and* a second nucleic acid encoding SEQ ID NO:4, 45, 47, or 50, does not reasonably provide enablement for a single element of and/or the combination of nucleic acids of a nucleic acid comprising all first nucleic acids encoding proteins having at least 90% identity to SEQ ID NO:2 or 6 and having the activity as set forth in the claim and a second nucleic acid encoding proteins having at least 90% identity to SEQ ID NO:4, 45, 47, or 50.
- Regarding claims 157 (claims 178-180, and 208-216 dependent therefrom), 158-164, and 167-177, the specification, while being enabling for an expression vector comprising a first nucleic acid comprising a nucleic acid sequence encoding SEQ ID NO:2 or 6 *and* a second nucleic acid comprising the nucleic acid sequence of SEQ ID NO:3, 43, or 48 or a nucleic acid sequence encoding SEQ ID NO:4, 45,

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47, and 50, does not reasonably provide enablement for a single element of and/or the combination of nucleic acids of an expression vector comprising a first nucleic acid comprising all nucleic acid sequences encoding proteins having at least 90% identity to SEQ ID NO:2 or 6, and optionally fragments of SEQ ID NO:2 or 6 as set forth in claims 158-161 and having the activity as set forth in the claim *and* a second nucleic acid comprising a nucleic acid sequence comprising the nucleic acids of claims 137 or 149 and optionally fragments or homologues of SEQ ID NO:4, 45, 47, or 50 as set forth in claims 164, 167, and 168, and 177.

- Regarding claims 181 (claims 195-197 and 208-216 dependent therefrom), 182-194 the specification, while being enabling for an expression vector comprising a first nucleic acid of SEQ ID NO:1 or 5 *and* a second nucleic acid comprising the nucleic acid sequence of SEQ ID NO:3, 43, or 48 or a nucleic acid sequence encoding SEQ ID NO:4, 45, 47, and 50, does not reasonably provide enablement for a single element of and/or the combination of nucleic acids in an expression vector comprising a first nucleic acid comprising all nucleic acids comprising a coding sequence of a cDNA that hybridize to an undefined number of nucleotides or the recited fragments of the complement of SEQ ID NO:1 or 5 *and* a second nucleic acid comprising a nucleic acid sequence comprising the nucleic acids of claims 137 or 149 and optionally variants and fragments of SEQ ID NO:4, 45, 47, or 50 or homologues of SEQ ID NO:3, 43, or 48.

Undue experimentation is required for a skilled artisan to make and/or use the entire scope of claimed nucleic acids, expression vectors, and host cells. Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s). The Factors most relevant to this rejection are addressed below.

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- The breadth of the claims: The claims are so broad as to encompass all nucleic acids and host cells comprising said nucleic acids as described above as being un-enabled by the instant specification. The scope of the claims is *not* commensurate with the enablement provided by the disclosure with regard to the large number of nucleic acids, expression vectors, and host cells broadly encompassed by the claims. In this case, the specification is enabling for a nucleic acid encoding SEQ ID NO:4, 45, 47, and 50; the nucleic acids of SEQ ID NO:3, 43, and 48; a nucleic acid comprising a first nucleic acid encoding SEQ ID NO:2 or 6 *and* a second nucleic acid encoding SEQ ID NO:4, 45, 47, or 50; an expression vector comprising a first nucleic acid comprising a nucleic acid sequence encoding SEQ ID NO:2 or 6 *and* a second nucleic acid comprising the nucleic acid sequence of SEQ ID NO:3, 43, or 48 or a nucleic acid sequence encoding SEQ ID NO:4, 45, 47, and 50, an expression vector comprising a first nucleic acid of SEQ ID NO:1 or 5 *and* a second nucleic acid comprising the nucleic acid sequence of SEQ ID NO:3, 43, or 48 or a nucleic acid sequence encoding SEQ ID NO:4, 45, 47, and 50.
- The lack of guidance and working examples: The specification in combination with the prior art and the knowledge of a skilled artisan fails to enable the entire scope of claimed variants and homologues of the nucleic acids of SEQ ID NO:1, 3, 5, 43, 48 or nucleic acids encoding variants and homologues of SEQ ID NO:4, 45, 47, and 50 as encompassed by the claims. For example, the specification provides no guidance as to those nucleotides and/or encoded amino acids that are necessary for kinase activity of the small subunit, subunit interaction between the large and small subunits, or promoting transcriptional elongation of the combined large and small subunits. Such guidance is necessary for a skilled artisan to generate the claimed nucleic acids and host cells with an expectation of obtaining an expressed polypeptide having the desired activity.
- The unpredictability of the art: Due to the inadequate guidance provided in the specification, one of skill in the art would recognize the high degree of unpredictability in generating the entire scope of claimed nucleic acids with an expectation of the encoded protein having the desired biological activity. Since the nucleic acid sequence of an encoding nucleic acid determines an encoded protein's structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid

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sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the encoded protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. One of skill in the art recognizes that alteration of a protein's encoding nucleic acid may have various unpredictable effects including loss of function. For example, Peng et al. (*J Biol Chem* 273:13855-13860) teach the generation of a kinase negative mutant of P-TEFb by mutating aspartate at position 199 of the small subunit to an asparagine (see page 13856, left column, middle). Furthermore, the unpredictability is compounded for obtaining an active enzyme complex of variant small *and* large subunits. For example, while a variant of the large subunit may interact with the small subunits represented by SEQ ID NO:4, 45, 47, or 50, it is highly unpredictable as to whether said variant of the large subunit would interact with *variants* of SEQ ID NO:4, 45, 47, or 50.

- The quantity of experimentation necessary: While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims. Given the lack of guidance and the high degree of unpredictability present, the experimentation necessary for a skilled artisan to make and use the entire scope of claimed nucleic acids, expression vectors, and host cells is far from routine.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological

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characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

[14] It appears that applicants' amendment has overcome all previous rejections under 35 USC 112, first paragraph, scope of enablement except for the rejection at item 15 of Paper No. 16. Applicants traverse the rejection (see item VII beginning at page 17 of Paper No. 20) by arguing that the concerns were addressed during an interview and an agreement was reached to overcome the rejection. However, applicants' amendment has not overcome the instant rejection for the reasons set forth in item 13 above.

Conclusion

[15] Claims 110, 113, 116-127, 133-143, 147-155, 157-164, and 167-172, 174-208, and 211-216 are rejected.

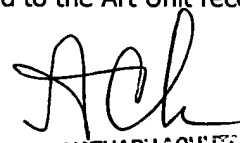
[16] Claims 111, 112, 128-132, 144-146, and 156 are objected to as being dependent upon a rejected base claim.

[17] Claims 110, 113, 116-127, 133-143, 147-155, 157-164, and 167-172, 174-208, and 211-216 would appear to be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

[18] The examiner requests that applicants provide a copy of all pending claims in the response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Thursday from 6:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for official papers filed to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (703) 746-5078. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652


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